

## DETAILED ACTION

Receipt and entry of the amendment dated 9/15/2011 is acknowledged.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless —

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 8-10, and 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Marcello et al (Res. Vir., 1998). This rejection is maintained for reasons set forth in the Office Action dated 3/15/2011, and for reasons set forth below.

The claims have been amended to recite that the IRES promotes expression of the positive selection marker. Such is an intended use limitation of the instant product claims. See, e.g., *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). (MPEP 2111.02). Furthermore, the instant specification provides no limiting definition of the phrase “promotes the translation of.” Thus, the phrase is given a broad interpretation to include literally any involvement, be it direct or indirect, of an IRES in the translation of the positive selection marker. Marcello et al clearly understood that in the relevant expression cassette, the IRES influenced expression (i.e. influenced either one or both of transcription and translation) of both the *hprt* and *TK* genes. See the legend of Fig. 1. It is considered that, at the least, the IRES “promoted translation” of the *hprt* gene by allowing it to be transcribed in conjunction with the *TK* gene.

***Response to Arguments***

Applicant's arguments filed 9/15/2011 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the teachings of Marcello et al involve only the translation of *TK* by the IRES, and thus do not teach the instant claim limitation that the IRES must "promote translation" of the positive selection marker; 2) the art recognizes that a positive selection marker downstream of the mutation target would require a fully functional mRNA; 3) *TK* is not to be considered a positive selection marker.

Regarding 1), this is not convincing for reasons set forth above. The claims are not so limited as applicants assert due to the broad interpretation of the intended use phrase "promotes translation."

Regarding 2), perhaps, but the issue is moot. The positive selection marker (*hpt*) in this instance is upstream of the mutational target (*TK*). Further, many of the cells of Marcello et al clearly expressed both *hpt* and *TK*, thus, full length mRNA was transcribed. Applicants reasoning here is less than clear.

Regarding 3), this has never been asserted by the Examiner.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 6-11, 13-15 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Galipeau et al (WO 00/65034, 11/2/2000) in view of Naldini et al (PNAS, 1996), Marcello et al (Res. Vir., 1998, as above) and Mansky et al (J. Virol., 2003 of record). **This rejection is**

**maintained for reasons set forth in the Office Action dated 3/15/2011. New claims and prior art have been added, necessitated by amendment of the claims.**

The teachings of Galipeau, Marcello and Naldini et al are applied as before. In addition, Naldini teaches the positive selection marker to be translated by the IRES (see, e.g. Figs. 1B and 9B, teaching the order CMV-TK-IRES-EGFP).

Mansky et al teach an HIV-1 vector having an expression cassette driven by the SV40 promoter comprising the *lacZ* mutational target gene and the neomycin positive selection marker translated by an IRES. See in particular Fig. 1 A.

The claimed vectors are essentially disclosed by Galipeau et al with the exception of the limitations wherein the positive selection marker is *hpt* (and the lentivirus-based limitation, addressed in the previous Office Action). The ordinary skilled artisan, seeking a viral gene therapy vector to deliver the *TK* gene of Galipeau et al, would have been motivated to use the *hpt* gene of Marcello et al in place of the EGFP of Galipeau et al because Marcello et al teaches *hpt* to be an alternative selection marker for selecting mammalian cells comprising the vector, i.e. the same purpose for which Galipeau et al used EGFP (and for which Mansky et al use the neomycin positive selection marker). Furthermore, both Galipeau and Mansky et al teach the utility of placing the positive selection marker after the IRES in the expression cassette. It would have been obvious for the skilled artisan to do this because of the known benefit of generating retro- or lentiviral vectors for delivery of transgenes as taught by both Galipeau and Naldini et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the

ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

***Response to Arguments***

Applicant's arguments filed 9/15/2011 have been fully considered but they are not persuasive. Applicants essentially assert that the EGFP of Galipeau et al is not to be considered a positive selection marker, and point to ¶ [0027] of the published application (US 20070042352 A1, the specification as filed has no paragraph numbering) as an alleged definition of a "positive selection marker." Such is not convincing given a reasonable interpretation of applicants attempts to define a positive selection marker and the use of EGFP by Galipeau et al to select cells expressing the protein. Cells expressing EGFP were sorted by FACS by Galipeau et al, meaning those that expressed EGFP were retained for further experiments, i.e. "permitted to live" in the presence of a selectable agent (the FACS sorting). Further, this follows applicants' assertions that the positive selection marker "distinguish cells that do not express the selectable marker", as Galipeau et al clearly used EGFP for this very purpose: cells not expressing EGFP were not collected from the FACS sorter.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL BURKHART whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/  
Primary Examiner, Art Unit 1633